CLAIMS

What is claimed is:

1. A method for preparing submicron sized particles of an organic compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent which is aqueous, the process comprising the steps of:

(i) dissolving the organic compound in the water-miscible first solvent to form a solution, the first solvent being selected from the group consisting of N-methyl-2-pyrrolidinone, 2-pyrrolidone, dimethyl sulfoxide, dimethylacetamide, lactic acid, methanol, ethanol, isopropanol, 3-pentanol, n-propanol, glycerol, butylene glycol, ethylene glycol, propylene glycol, mono- and diacylated monoglycerides, dimethyl isosorbide, acetone, dimethylformamide, 1,4-dioxane, polyethylene glycol, polyethylene glycol esters, polyethylene glycol sorbitans, polyethylene glycol monoalkyl ethers, polypropylene glycol, polypropylene alginate, PPG-10 butanediol, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-15 stearyl ether, propylene glycol dicaprylate, propylene glycol dicaprate, propylene glycol laurate;

(ii) mixing the solution with the second solvent to define a pre-suspension; and

(iii) adding energy to the pre-suspension to form particles having an average effective particle size of less than about 2μm.

2. The method of claim 1 further comprising the step of:

mixing into the second solvent a first surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

3. The method of claim 2 wherein the nonionic surfactant is selected from the group consisting of: polyoxyethylene fatty alcohol ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polysaccharides, starch, starch derivatives, hydroxyethylstarch, polyvinyl alcohol, and polyvinylpyrrolidone.

4. The method of claim 2 wherein the anionic surfactant is selected from the group consisting of: potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium

sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts, cholic acid, deoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid, and calcium carboxymethylcellulose.

5. The method of claim 2 wherein the cationic surfactant is selected from the group consisting of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

6. The method of claim 2 wherein the surface active biological modifiers are selected from the group consisting of: albumin, casein, heparin, hirudin, or other proteins.

7. The method of claim 2 wherein the first solvent is N-methyl-2-pyrrolidinone.

8. The method of claim 7 wherein the anionic surfactant is a copolymer of oxyethylene and oxypropylene.

9. The method of claim 8 wherein the copolymer of oxyethylene and oxypropylene is a block copolymer.

10. The method of claim 2 further comprising the step of mixing into the second solvent a second surface modifier.

11. The method of claim 10 wherein the second surface modifier is selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

12. The method of claim 11 wherein the second surface modifier is a bile salt or a salt thereof.

13. The method of claim 11 wherein the second surface modifier is selected from deoxycholic acid, glycocholic acid, glycodeoxycholic acid, taurocholic acid and salts of these acids.

14. The method of claim 2 further comprising the step of adding a pH adjusting agent to the second solvent.

15. The method of claim 14 wherein the pH adjusting agent is selected from the group consisting of sodium hydroxide, hydrochloric acid, tris buffer, citrate buffer, acetate, lactate, and meglumine.

16. The method of claim 14 wherein the pH adjusting agent is added to the second solvent to bring the pH of the second solvent within the range of from about 3 to about 11.

17. The method of claim 1 further comprising the step of:

mixing into the solution a third surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

18. The method of claim 17 wherein the nonionic surfactant of the third surface modifier is selected from the group consisting of: polyoxyethylene fatty alcohol ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polysaccharides, starch, starch derivatives, hydroxyethylstarch, polyvinyl alcohol, and polyvinylpyrrolidone.

19. The method of claim 17 wherein the anionic surfactant of the third surface modifier is selected from the group consisting of: potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts and calcium carboxymethylcellulose.

20. The method of claim 17 wherein the cationic surfactant of the third surface modifier is selected from the group consisting of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

21. The method of claim 17 wherein the surface active biological modifiers are selected from the group consisting of: albumin, casein, heparin, hirudin, or other proteins.

22. The method of claim 17 wherein the first solvent is N-methyl-2-pyrrolidinone.

23. The method of claim 22 wherein the third surface modifier is a copolymer of oxyethylene and oxypropylene.

24. The method of claim 23 wherein the copolymer of oxyethylene and oxypropylene is a block copolymer.

25. The method of claim 17 further comprising the step of mixing into the solution a fourth surface modifier.

26. The method of claim 25 wherein the fourth surface modifier is selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

27. The method of claim 26 wherein the fourth surface modifier is a nonionic surfactant is selected from the group consisting of: polyoxyethylene fatty alcohol ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polysaccharides, starch, starch derivatives, hydroxyethylstarch, polyvinyl alcohol, and polyvinylpyrrolidone.

28. The method of claim 26 wherein the fourth surface modifier is an anionic surfactant selected from the group consisting of: potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts and calcium carboxymethylcellulose.

29. The method of claim 26 wherein the fourth surface modifier is a cationic surfactant selected from the group consisting of: of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

30. The method of claim 26 wherein the surface active biological modifiers are selected from the group consisting of: albumin, casein, heparin, hirudin, or other proteins.

31. The method of claim 17 further comprising the step of:

mixing into the second solvent a fifth surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

32. The method of claim 31 wherein the fifth surface modifier is a nonionic surfactant selected from the group consisting of: polyoxyethylene fatty alcohol ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polysaccharides, starch, starch derivatives, hydroxyethylstarch, polyvinyl alcohol, and polyvinylpyrrolidone.

33. The method of claim 31 wherein the fifth surface modifier is an anionic surfactant selected from the group consisting of: potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts and calcium carboxymethylcellulose.

34. The method of claim 31 wherein the fifth surface modifier is a cationic surfactant selected from the group consisting of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

35. The method of claim 31 wherein the surface active biological modifiers are selected from the group consisting of: albumin, casein, heparin, hirudin, or other proteins.

36. The method of claim 31 wherein the first solvent is N-methyl-2-pyrrolidinone.

37. The method of claim 36 wherein the fifth surface modifier is a copolymer of oxyethylene and oxypropylene.

38. The method of claim 37 wherein the copolymer of oxyethylene and oxypropylene is a block copolymer.

39. The method of claim 31 further comprising the step of mixing into the solution a sixth surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

40. The method of claim 1 further comprising the step of:

mixing into the second solvent a phospholipid.

41. The method of claim 40 wherein the phospholipid is selected from natural phospholipids and synthetic phospholipids.

42. The method of claim 40 wherein the phospholipid is selected from the group consisting of: phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, lysophospholipids, egg phospholipid and soybean phospholipid.

43. The method of claim 40 further comprising the step of mixing into the solution a seventh surface modifier selected from anionic surfactants, cationic surfactants and non-ionic surfactants.

44. The method of claim 43 wherein the nonionic surfactant of the seventh surface modifier is selected from the group consisting of: polyoxyethylene fatty alcohol ethers,

polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polysaccharides, starch, starch derivatives, hydroxyethylstarch, polyvinyl alcohol, and polyvinylpyrrolidone.

45. The method of claim 43 wherein the anionic surfactant of the seventh surface modifier is selected from the group consisting of: potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts and calcium carboxymethylcellulose.

46. The method of claim 43 wherein the cationic surfactant of the seventh surface modifier is selected from the group consisting of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

47. The method of claim 43 wherein the surface active biological modifiers are selected from the group consisting of: albumin, casein, heparin, hirudin, or other proteins.

48. The method of claim 43 wherein the seventh surface modifier is a bile acid or a salt thereof.

49. The method of claim 43 wherein the first solvent is N-methyl-2-pyrrolidinone.

50. The method of claim 49 further comprising the step of adding a phospholipid to the second solvent.

51. The method of claim 50 wherein the phospholipid is selected from natural phospholipids and synthetic phospholipids.

52. The method of claim 50 wherein the phospholipid is selected from the group consisting of: phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, lysophospholipids, egg phospholipid and soybean phospholipid.

53. The method of claim 50 further comprising the step of mixing into the solution an eighth surface modifier selected from anionic surfactants, cationic surfactants and non-ionic surfactants.

54. The method of claim 53 wherein the nonionic surfactant of the eighth surface modifier is selected from the group consisting of: polyoxyethylene fatty alcohol ethers, sorbitan fatty acid esters, polyoxyethylene fatty acid esters, sorbitan esters, glycerol monostearate, polyethylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, poloxamers, polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polyvinyl alcohol, and polyvinylpyrrolidone.

55. The method of claim 53 wherein the anionic surfactant of the eighth surface modifier is selected from the group consisting of: potassium laurate, triethanolamine stearate, sodium lauryl sulfate, sodium dodecylsulfate, alkyl polyoxyethylene sulfates, sodium alginate, dioctyl sodium sulfosuccinate, phosphatidyl glycerol, phosphatidyl inositol, phosphatidylserine, phosphatidic acid and their salts, glyceryl esters, sodium carboxymethylcellulose, bile acids and their salts and calcium carboxymethylcellulose.

56. The method of claim 53 wherein the cationic surfactant of the eighth surface modifier is selected from the group consisting of quaternary ammonium compounds, benzalkonium chloride, cetyltrimethylammonium bromide, chitosans and lauryldimethylbenzylammonium chloride.

57. The method of claim 53 wherein the surface active biological modifiers are selected from the group consisting of: albumin, casein, heparin, hirudin, or other proteins.

58. The method of claim 53 wherein the eighth surface modifier is a bile acid or a salt thereof.

59. The method of claim 58 wherein the first solvent is N-methyl-2-pyrrolidinone.

60. A method for preparing submicron sized particles of an organic compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent which is aqueous, the process comprising the steps of:

(i) dissolving the organic compound in the water-miscible first solvent to form a solution, the first solvent being selected from the group consisting of N-methyl-2-pyrrolidinone, 2-pyrrolidone, dimethyl sulfoxide, dimethylacetamide, lactic acid, methanol, ethanol, isopropanol, 3-pentanol, n-propanol, glycerol, butylene glycol, ethylene glycol, propylene glycol, mono- and diacylated monoglycerides, dimethyl isosorbide, acetone, dimethylformamide, 1,4-dioxane,ethyl acetate, propyl acetate, polyethylene glycol, polyethylene glycol esters, polyethylene glycol sorbitans, polyethylene glycol monoalkyl ethers, polypropylene glycol, polypropylene alginate, PPG-10 butanediol, PPG-10 methyl

glucose ether, PPG-20 methyl glucose ether, PPG-15 stearyl ether, propylene glycol dicaprylate, propylene glycol dicaprate, propylene glycol laurate;

(ii) mixing the solution with the second solvent to define a pre-suspension wherein the organic compound is in an amorphous form, a semicrystalline form or in a supercooled liquid form as determined by DSC and having an average effective particle size; and

(iii) annealing the pre-suspension to form particles having essentially the same average effective particle size of the pre-suspension and in a more stable form.

61. The method of claim 60 wherein the annealing step includes the step of converting the particles of the pre-suspension to a crystalline form as determined by DSC.

62. The method of claim 60 wherein the particles after the annealing step have a reduced tendency to aggregate into larger particles when compared to the particles of the pre-suspension.

63. The method of claim 60 wherein the particles of the pre-suspension have an average effective particle size of less than about 2μm.

64. The method of claim 60 wherein the particles of the pre-suspension have an average effective particle size of from about 2μm to about 50 nm.

65. The method of claim 60 wherein the particles of the pre-suspension have an average effective particle size of less than about 400 nm.

66. A method for preparing submicron sized particles of an organic compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent which is aqueous, the process comprising the steps of:

(i) dissolving the organic compound in the water-miscible first solvent to form a solution, the first solvent being selected from the group consisting of N-methyl-2-pyrrolidinone, 2-pyrrolidone, dimethyl sulfoxide, dimethylacetamide, lactic acid, methanol, ethanol, isopropanol, 3-pentanol, n-propanol, glycerol, butylene glycol, ethylene glycol, propylene glycol, mono- and diacylated monoglycerides, dimethyl isosorbide, acetone, dimethylformamide, 1,4-dioxane, polyethylene glycol, polyethylene glycol esters, polyethylene glycol sorbitans, polyethylene glycol monoalkyl ethers, polypropylene glycol, polypropylene alginate, PPG-10 butanediol, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-15 stearyl ether, propylene glycol dicaprylate, propylene glycol dicaprate, propylene glycol laurate;

(ii) mixing the solution with the second solvent to define a pre-suspension of particles in a friable form; and

(iii) adding energy to the pre-suspension to form particles having an average effective particle size of less than about 2 μm.

67. The method of claim 66 further comprising the step of:

mixing into the second solvent a first surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and biological surface active molecules.

68. The method of claim 67 wherein the first solvent is N-methyl-2-pyrrolidinone.

69. The method of claim 68 wherein the anionic surfactant is a copolymer of oxyethylene and oxypropylene.

70. The method of claim 69 wherein the copolymer of oxyethylene and oxypropylene is a block copolymer.

71. The method of claim 67 further comprising the step of mixing into the second solvent a second surface modifier selected from the group consisting of anionic surfactants, cationic surfactants, nonionic surfactants and biological surface active molecules.

72. The method of claim 71 wherein the second surface modifier is a bile salt or a salt thereof.

73. The method of claim 71 wherein the second surface modifier is selected from deoxycholic acid, glycocholic acid, glycodeoxycholic acid, taurocholic acid and salts of these acids.

74. The method of claim 67 further comprising the step of adding a pH adjusting agent to the second solvent.

75. The method of claim 74 wherein the pH adjusting agent is selected from the group consisting of sodium hydroxide, hydrochloric acid, tris buffer, citrate buffer, acetate, lactate, and meglumine.

76. The method of claim 74 wherein the pH adjusting agent is added to the second solvent to bring the pH of the second solvent within the range of from about 3 to about 11.

77. The method of claim 66 further comprising the step of:

mixing into the solution a third surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and biological surface active molecules.

78. The method of claim 77 wherein the first solvent is N-methyl-2-pyrrolidinone.

79. The method of claim 78 wherein the third surface modifier is a copolymer of oxyethylene and oxypropylene.

80. The method of claim 79 wherein the copolymer of oxyethylene and oxypropylene is a block copolymer.

81. The method of claim 77 further comprising the step of mixing into the solution a fourth surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and biological surface active molecules.

82. The method of claim 77 further comprising the step of:

mixing into the second solvent a fifth surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and biological surface active molecules.

83. The method of claim 82 wherein the first solvent is N-methyl-2-pyrrolidinone.

84. The method of claim 83 wherein the fifth surface modifier is a copolymer of oxyethylene and oxypropylene.

85. The method of claim 82 further comprising the step of mixing into the solution a sixth surface modifier selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and biological surface active molecules.

86. The method of claim 66 further comprising the step of:

mixing into the second solvent a phospholipid.

87. The method of claim 86 wherein the phospholipid is selected from natural phospholipids and synthetic phospholipids.

88. The method of claim 86 wherein the phospholipid is selected from the group consisting of: phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, lysophospholipids, egg phospholipid and soybean phospholipid.

89. The method of claim 86 further comprising the step of mixing into the solution a seventh surface modifier selected from anionic surfactants, cationic surfactants, non-ionic surfactants and biological surface active molecules.

90. The method of claim 89 wherein the seventh surface modifier is a bile acid or a salt thereof.

91. The method of claim 90 wherein the first solvent is N-methyl-2-pyrrolidinone.

92. The method of claim 91 further comprising the step of adding a phospholipid to the second solvent.

93. The method of claim 92 wherein the phospholipid is selected from natural phospholipids and synthetic phospholipids.

94. The method of claim 92 wherein the phospholipid is selected from the group consisting of: phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, lysophospholipids, egg phospholipid and soybean phospholipid.

95. The method of claim 92 further comprising the step of mixing into the solution an eighth surface modifier selected from anionic surfactants, cationic surfactants, non-ionic surfactants and biological surface active molecules.

96. The method of claim 95 wherein the eighth surface modifier is a bile acid or a salt thereof.

97. The method of claim 96 wherein the first solvent is N-methyl-2-pyrrolidinone.

98. A method for preparing a suspension of a pharmaceutically-active compound, the solubility of which is greater in a water-miscible first organic solvent than in a second solvent which is aqueous, the process comprising the steps of:

(i) dissolving a first quantity of the pharmaceutically-active compound in the water-miscible first organic solvent to form a first solution;

(ii) mixing the first solution with the second solvent to precipitate the pharmaceutically-active compound to create a pre-suspension; and

(iii) seeding the first solution or the second solvent prior to the or the pre-suspension after the mixing step.

99. The method of claim 98 wherein the step of precipitating the pharmaceutically-active compound comprises the step of precipitating the compound in a form selected from the group consisting of a supercooled liquid, an amorphous particle, a semicrystalline particle and a crystalline particle.

100. The method of claim 99 further comprising the step of adding energy to the pre-suspension.

101. The method of claim 100 wherein the adding-energy step comprises the step of subjecting the pre-suspension to high energy agitation.

102. The method of claim 100 wherein the adding-energy step comprises the step of adding heat to the pre-suspension.

103. The method of claim 100 wherein the energy-addition step comprises the step of exposing the pre-suspension to electromagnetic energy.

104. The method of claim 103 wherein the step of exposing the pre-suspension to electromagnetic energy comprises the step of exposing the pre-suspension to a laser beam.

105. The method of claim 98 further comprising the step of forming a desired polymorph of the pharmaceutically active compound.

106. The method of claim 105 wherein the step of seeding comprises the step of using a seed compound.

107. The method of claim 105 wherein the seed compound is the desired polymorph of the pharmaceutically-active compound.

108 The method of claim 105 wherein the seed compound is a compound other than the desired polymorph of the pharmaceutically-active compound.

109. The method of claim 108 wherein the seed compound is selected from the group consisting of: an inert impurity; and an organic compound with a structure similar to that of the desired polymorph.

110. The method of claim 105 wherein the seed compound is added to the first solution.

111. The method of claim 105 wherein the seed compound is added to the second solvent.

112. The method of claim 105 wherein the seed compound is added to the pre-suspension.

113. The method of claim 104 wherein the step of forming a desired polymorph comprises the step of forming a seed compound in the first solution.

114. The method of claim 113 wherein the step of forming the seed compound in the first solution comprises the step of adding the pharmaceutically-active compound in sufficient quantity to exceed the solubility of the pharmaceutically-active compound in the first solvent to create a supersaturated solution.

115. The method of claim 114 wherein the step of forming the seed compound in the first solution further comprises the step of treating the supersaturated solution.

116. The method of claim 115 wherein the step of treating the supersaturated solution comprises the step of aging the supersaturated solution.

117. The method of claim 116 wherein the seeding step comprises the step of using electromagnetic energy.

118. The method of claim 117 wherein the electromagnetic energy is dynamic electromagnetic energy.

119. The method of claim 117 wherein the electromagnetic energy is a laser beam.

120. The method of claim 117 wherein the electromagnetic energy is radiation.

121. The method of claim 98 wherein the step of seeding comprises the step of using a particle beam.

122. The method of claim 98 wherein the step of seeding comprises the step of using an electron beam.

123. The method of claim 98 wherein the step of seeding comprises using ultrasound.

124. The method of claim 98 wherein the step of seeding comprises using a static electrical field.

125. The method of claim 98 wherein the step of seeding comprises using a static magnetic field.

126. The method of claim 98 further comprising the steps of forming particles having an average effective particle size less than about 2μm.

127. A composition of matter of a polymorphic pharmaceutically-active compound in a desired polymorphic form essentially free of an unspecified polymorphic form.

128. The composition of claim 127 wherein the pharmaceutically-active compound is itraconazole.